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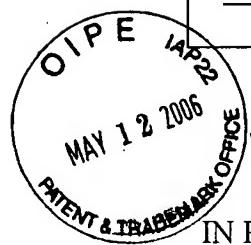
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## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF

**DANPING LI, ET AL**APPLICATION NO: **10/023,533**FILED: **12/17/2001**FOR: **ANTIDIABETIC FORMULATION AND METHOD**ART UNIT: **1614**EXAMINER: **KWON, BRIAN YONG S**

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APPEAL BRIEF

Sir:

This is an appeal from the Final Office Action mailed November 2, 2005 where Claims 1 and 11 to 16 of the above-identified application are finally rejected.

## (1) REAL PARTY IN INTEREST

The real party in interest in this appeal is Bristol-Myers Squibb Company, a Delaware corporation, having a place of business at Lawrenceville-Princeton Road, Princeton, NJ 08543-4000. Bristol-Myers Squibb Company is the assignee and owner of the entire interest in the above-identified application by virtue of an assignment filed in the subject application, which was recorded in the United States Patent and Trademark Office on December 17, 2001 at Reel/Frame 012406/0925 (copy of the Notice of Recordation of Assignment being enclosed herewith).

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PATENT TRADEMARK OFFICE

## (2) RELATED APPEALS AND INTERFERENCES

The undersigned knows of no other appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

## (3) STATUS OF CLAIMS

Claims 1 and 11 to 16 have been finally rejected and are under appeal.

## (4) STATUS OF AMENDMENTS

The Claims on appeal have not been amended after final rejection.

## (5) SUMMARY OF CLAIMED SUBJECT MATTER

Appellants' invention as defined in independent Claim 1 is directed to a pharmaceutical composition which is a single dosage formulation in the form of a tablet containing metformin and glipizide which formulation contains 2 to 3% moisture, and including an outer protective coat or finishing layer surrounding the tablet, the formulation being designed to control moisture so that the glipizide does not hydrolyze and the metformin is compressible. Appellants' formulation as claimed in Claim 1 is devoid of an enteric coating. It is not and cannot be a sustained or controlled release formulation without an enteric coating.

Claims 11 and 13 to 16 depend from Claim 1 and define dosages of metformin and glipizide.

Claim 12 depends from Claim 1 and defines a weight ratio of metformin to glipizide.

## (6) GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Appellants' composition as defined in Claims 1 and 11 to 16 is finally rejected over 35 U.S.C. §103(a) as being unpatentable over Chen et al. (U.S. Patent No. 6,099,862) in view of Patel et al. (U.S. Patent No. 6,248,363) and Bonhomme et al. (U.S. Patent NO. 6,303,146).

## (7) ARGUMENT

### Obviousness under 35 U.S.C. §103

A determination of obviousness under 35 U.S.C. §103 is a legal conclusion based upon factual evidence. The factual inquiries on which the conclusion is based are those defined in

Graham v. John Deere Co., 383 U.S. 1 (1966), and restated in Hybritech, Inc. v. Monoclonal Antibodies, Inc., 231 U.S.P.Q. 81 (Fed. Cir. 1986), cert. den. 107 S. Ct. 1606 (1987). These factual inquiries are:

- (1) determining the scope and content of the prior art;
- (2) ascertaining the differences between the invention and the prior art and the claims at issue,
- (3) resolving the level of ordinary skill in the pertinent art, and
- (4) considering objective evidence present in the application indicating obviousness or nonobviousness.

Obviousness is tested by what the combined teachings of the prior art references would have suggested to those of ordinary skill in the art, not by whether it might have been "obvious to try" a particular combination of elements from the prior art (In re Fine, 5 U.S.P.Q. 2d 1596 (Fed. Cir. 1988); In re Wiggins, 158 U.S.P.Q. 199 (1968); In re Mercier, 185 U.S.P.Q. 774 (1976); In re Antoine, 195 U.S.P.Q. 6 (1977); In re Goodwin, Margrave and Wagner, 198 U.S.P.Q. 1 (1978); In re Yates, 211 U.S.P.Q. 1149 (1981)). The teachings of the prior art can only be combined if there is some suggestion or incentive in the prior art to do so (ACS Hospital Systems, Inc. v. Montefiore Hosp. et al.; 221 U.S.P.Q. 929 (CAFC 1984)).

Further, as stated in W.L. Gore & Assoc., Inc. v. Garlock, Inc., 220 U.S.P.Q. 303 (Fed. Cir. 1984):

To imbue one of ordinary skill in the art with knowledge of the invention . . . , when no prior art reference or references . . . convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher.

Applying the above law, it will be seen that Appellants' invention as claimed in Claims 1 and 11 to 16 is patentable over the cited references each taken alone or in combination.

The Examiner contends that:

"Chen teaches combination of biguanide (i.e., metformin) and sulfonylurea (i.e., glipizide, glyburide (=glibenclamide), gliclazide, tolazamide, tolbutamide and etc...), namely a pharmaceutical tablet containing combination of metformin and glipizide, wherein core of said composition is prepared by mixing metformin and glipizide with povidone, sodium lauryl sulfate and magnesium stearate and then tablet is seal coated with an opadry materials (column 3, lines 6-21; Examples 1-2). As specific embodiments of the claimed invention, Examples (1-2) discloses 850mg or

500mg of metformin HCl and 5 mg of glipizide controlled release tablet, wherein granules containing metformin and glipizide are dried ‘in the fluidized bed coater until the loss on drying is less than 2%’ and then compressed to tablet.”

“Patel is being supplied as a reference to demonstrate the routine knowledge in art in preparing pharmaceutical actives such as metformin and glipizide in various pharmaceutical delivery systems including various dosage forms (e.g., tablet, capsule, quick or fast dissolving tablet, granule, etc...); coated with various coating methods (e.g., enteric coating, seal coating, protected coating or layered coating, etc...); and dosage form release system (e.g., immediate release pulsatile release, controlled release, extended release, delayed release, targeted release). See column 6, line 32; column 7, line 7; column 9, line 33 and 66; column 10, line 31; column 41, line 29 thru column 51, line 10.”

“Bonhomme discloses the combination of biguanidines (i.e., metformin) and sulfonylurea (i.e., glibenclamide (=glyburide), gliclazide, glipizide, tobutamide, tolazamide, gliquidone and chlorpropamide), namely combination of metformin and glibenclamide, wherein said combination is prepared in solid oral dosage form (i.e., tablet), and wherein said tablet is coated with hydrophilic cellulose polymer (column 1, lines 11-21; column 2, line 45 thru column 3, line 57). In addition, Bonhomme teaches the routine knowledge in maintaining 2-3% w/w moisture content prior to ‘tableting’ (column 6, lines 37-49).”

“The teaching of Chen differs from the claimed invention in ‘being devoid of an enteric coating’; ‘2 to 3% by weight moisture’; and the specific dosage amounts of metformin and glipizide in said composition. However, it would have been obvious in view of Patel (US 6248363 B1) who teaches pharmaceutical delivery systems for pharmaceutical active ingredients including metformin and glipizide, wherein said active ingredients can be prepared in various dosage forms (e.g., tablet, capsule, quick or fast dissolving tablet, granule, etc...); coated with various coating methods (e.g., enteric coating, seal coating, protected coating or layered coating, etc...); and dosage form release system (e.g., immediate release, pulsatile release, controlled release, extended release, delayed release, targeted release), and Bonhomme who teaches the routine knowledge in art in determining 2-3% w/w moisture content prior to ‘tableting’.

“The above references in combination make clear that the combination of metformin and glipizide in single dosage formulation is old and well known in the art. The above references in combination also make clear that the preparation of pharmaceutical composition containing metformin and/or glipizide in various dosage forms (e.g., tablet, quick, fast dissolving tablet, capsule, etc...) coated with coating techniques (e.g., enteric coating, protective coating, seal coating, etc...) designed for various dosage form release systems (e.g., immediate release, controlled release, delayed release, etc...) is old and well known in the art. Furthermore, the above references in combination make clear that optimization of ‘less than 2%’ to ‘2 to 3%

'moisture' is well within the skill of the artisan. One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a)."

"With respect to the instantly required 'devoid of an enteric coating', Patel teaches that determination of appropriate dosage forms (e.g., tablet covered with enteric coating or with protective coating or finishing layer) having optimum therapeutic index is well considered within the skill of the artisan, and the artisan would be motivated to determine optimum dosage forms to maximize the effects of the drug. Therefore, the references in combination make obvious the claimed invention."

"With respect to the specific dosage amounts of active ingredients in said composition, those of ordinary skill in the art readily optimize effective dosages as determined by good medical practice and the clinical condition of the individual patient. Regardless of the manner of administration, the specific dose may be calculated according to body weight, body surface area or organ size. Further refinement of the calculations necessary to determine the appropriate dosage for treatment involving each of the above mentioned formulations is routinely made by those of ordinary skill in the art and is within the ability of tasks routinely performed by them without undue experimentation, especially in light of the dosage information in column 5, lines 1-15."

It is submitted that Appellants' invention claimed in Claims 1 and 11 to 16 is patentable over Chen et al. taken above.

Chen et al. disclose a controlled release tablet which, as disclosed in Example 1, may include a combination of metformin HCl (800 mg) and glipizide (5 mg) in a tablet core and as disclosed in Example 2, may include a combination of metformin HCl (500 mg) and glipizide (5 mg) in a tablet core. The Chen et al. Examples 1 and 2 tablet cores include a seal coating (optional) and a sustained release coating surrounding the cores, which sustained release coating is formed of a semi-permeable membrane which as an enteric coat provides for the controlled release of drugs and which will prevent release of drug prior to reaching the intestines. The sustained release coating (semi-permeable membrane of Chen et al.) includes one hole drilled onto each side of the sustained release tablet, which holes allow for release of drugs into the intestines. As indicated in Examples 1 and 2 (Col. 7, lines 4-5 and Col. 8, lines 25 to 26) of Chen et al., the Chen et al. tablet is tested in simulated intestinal fluid which indicates that the tablet is expected to release drug in the intestines and not the stomach. This means that the Chen et al. semi-permeable membrane is an enteric coat. It is also

apparent that the seal coat of Chen et al. is not an enteric coat since Chen et al. already has one enteric coat, namely, the semi-permeable membrane.

As indicated in Column 3, lines 61 to 64 of Chen et al.,

“The semipermeable membrane is permeable to the passage of an external fluid such as water . . .”

Appellants' tablet as claimed must contain at least 2% moisture so that it is compressible but no more than 3% moisture so that the glipizide will not hydrolyze. Such a semi-permeable membrane of Chen et al. which includes holes to allow release of drugs will not control moisture as required by Appellants' Claim 1. Appellants use the outer protective coating to control moisture content.

Appellants' tablets include an outer protective layer to prevent moisture from seeping into the tablet and is not a semi-permeable membrane permeable to water (Col. 3, lines 61 to 63, Chen et al.). The Chen et al. semi-permeable membrane is actually an enteric coating as seen by the fact that the Chen et al. tablet is tested in simulated intestinal fluid (Col. 7, lines 4-5, Col. 8, lines 25 to 33) and not in stomach acid. An enteric coat prevents release of drug prior to reaching the intestines.

The outer protective coating or finishing layer is not an enteric coating and will not serve to control or sustain release of the metformin and/or glipizide, but only serves to protect the tablet from physical abrasion and prevent contact of the drug with liquids which cause premature dissolution and release of drug before it is ingested or before it is swallowed. The outer protective coating acts as a barrier against moisture and will minimize hydrolysis of the glipizide. See Example 1, page 26, lines 19 to 26 of the Specification.

The tablet cores of Examples 1 and 2 of Chen et al. are formed by a granulation technique where granules containing metformin and glipizide “are dried in the fluidized bed coater until the loss on drying is less than 2%.”

It is submitted that Appellants' composition as claimed in Claims 1 and 11 to 16 are patentable over Chen et al. As indicated, in Claim 1, Appellants' tablets are devoid of an enteric coating. The Chen et al. tablets contain a sustained release layer which is a semi-permeable membrane which includes openings and thus are sustained release tablets, which as shown in Examples 1 and 2 release drugs over a 16 hour period. In fact, if Appellants employed a semi-permeable membrane as in Chen et al., instead of an outer protective coating, it could conceivably

cause Appellants' tablet to dry to less than 2% moisture or to absorb moisture to greater than 3%. This would defeat the purpose of Appellants' invention as defined in Claim 1. Appellants employ the outer protective coat and not a semi-permeable membrane as in Chen et al. Thus, Appellants' tablet as claimed is not a controlled release or sustained release tablet as disclosed by Chen et al.

Appellants' tablets must include sufficient moisture (2 to 3%) to leave the metformin sufficiently compressible so that tablets may be formed. In addition, if less than 2% moisture is present in Appellants' tablets, the tablets will disintegrate in that the crowns of the tablet will separate from the body (capping). However, the water content must not be greater than 3% to ensure that the glipizide will not be hydrolyzed.

There is no disclosure or suggestion in Chen et al. of a tablet which is devoid of an enteric coat and that contains 2 to 3% moisture.

There is nothing in Chen et al. which would motivate one skilled in the art to change the Chen et al. tablet (originally designed as a sustained release tablet with a semi-permeable membrane (permeable to water) which includes openings in the tablet to allow drugs to be released) to form a tablet which is devoid of an enteric coating and must contain 2-3% moisture.

Appellants' Claim 1 proviso "said composition being devoid of an enteric coating" excludes any possibility of having an "enteric coating". In addition, Appellants' tablet as claimed cannot include a semi-permeable membrane permeable to water since Appellants must control moisture content. This is Appellants' inventive concept. Thus, the inventive concept of Chen et al. to provide a controlled release tablet which allows water or other fluids to enter the tablets through specially designed openings in the semi-permeable membrane is totally different from Appellants' inventive concept of preventing moisture loss in a tablet to ensure a 2-3% moisture content to ensure tablet integrity and stability of glipizide.

The "outer protective coating or finishing layer surrounding said tablet" defined in Claim 1 is not an enteric coating or a semi-permeable membrane as used by Chen et al. and does not encompass an enteric coating or a semi-permeable membrane. Claim 1 defines the composition as being devoid of an enteric coating. Thus, the outer protective coating or finishing layer must be other than an enteric coating. In addition, Appellants' tablet must contain 2-3% moisture. The Chen et al. semi-permeable membrane allows water to penetrate the membrane and therefore would not be designed to control moisture as required in Appellants' Claim 1.

The term "enteric coat" generally refers to preventing a tablet from releasing drug not in the stomach but in the intestines where the enteric coat dissolves ([www.wholehealthmd.com/refshelf/glossary](http://www.wholehealthmd.com/refshelf/glossary)).

In fact, the Chen et al. semi-permeable membrane is an enteric coating. As seen in Column 7, lines 4-5 and Column 8, lines 25 to 53, it is indicated that the Chen et al. tablet is tested in simulated intestinal fluid. This indicates that the Chen et al. tablet will pass from the stomach into the intestines where the drug is released. Thus, the semi-permeable membrane acts as an enteric coating. If the Chen et al. semi-permeable membrane were not an enteric coating, the Chen et al. tablet would have been tested in stomach acid for drug release properties and not in simulated intestinal fluid.

In Appellants' Specification at page 9, lines 1 to 5 and at page 16, starting at line 25, "enteric coated glipizide particles" are disclosed (but are not claimed). It is also indicated that the enteric coated glipizide particles "may be further coated with an outer protective finishing coat or layer...." Appellants would not coat enteric coated particles with an enteric coating or a semi-permeable membrane. The protective finishing coat or layer is exactly that, a protective coat and not an enteric coat. Appellants' protective finishing coat or layer protects the composition from physical abrasion or premature contact with liquids or other materials which could possibly cause premature release of the drug. The protective finishing coating or layer functions to delay release of the drug before the dosage form is ingested or swallowed. Once swallowed, the protective coat does not delay or control release of drug in the body.

Protective finishing coat or layer is not encompassed by "enteric coat" which delays or controls release of drug.

In essence, the Examiner is attempting to totally redesign Chen et al. in view of the teachings of Appellants to construct a rejection which has no basis, in fact. Appellants' tablet is not a controlled release tablet whereas Chen et al. must be a controlled release tablet.

The differences between Appellants' invention as claimed and the tablet of Chen et al. are significant and unobvious so that the subject matter of Appellants' invention as a whole would not be obvious to one skilled in the art.

For the aforementioned reasons, it is submitted that Appellants' invention as claimed in Claims 1 and 11 to 16 is patentable over Chen et al.

The Examiner contends that:

"Unlike applicant's assertion, there is no indication in the present claims, however that said composition must be in the form of immediate release tablets. Applicant's recitation of 'being devoid of an enteric coating' does not render the claimed composition to be essentially in the form of immediate release tablet. Reading the instant claims with their 'broadest reasonable interpretation', the term 'outer protective coating or finishing layer surrounding said tablet, said composition being devoid of an enteric coating' is understood as coating outer surface of tablet with any known coating techniques of pharmaceutical compositions (e.g., seal coating, film coatings, barrier coatings, compress coatings, fast disintegrating coatings, or enzyme degradable coatings) except enteric coating. Therefore, regardless of Chen's delivering of said composition in sustained release tablet or immediate release tablet, Chen's disclosure of 'seal coated with an Opadry material or other suitable water-soluble material' to the tablet or core (see column 6, line 36-39; Example 2) 'metes and bounds' the claimed limitation."

The Chen et al. seal coat is indeed not an enteric coat and is not for controlling release of drug.

When Appellants' claims define their tablets as devoid of an enteric coating, they are stating that the tablet as claimed is not a controlled release or sustained release tablet since it does not include an enteric coating.

It is submitted that Appellants' invention as claimed in Claims 1 and 11 to 16 is patentable over U.S. Patent No. 6,248,363 to Patel et al. taken alone.

Patel et al. disclose solid pharmaceutical compositions which include a solid carrier, the solid carrier including a substrate and an encapsulation coat on the substrate, the encapsulation coat including at least one ionic or non-ionic hydrophilic surfactant and/or a lipophilic surfactant or a triglyceride, and a pharmaceutical active component. Other similar embodiments are disclosed as well, all of which much include an encapsulation coat which will contain the pharmaceutical active ingredient. Patel et al. discloses literally hundreds, if not thousands of drugs which may be used among which are glipizide and metformin. However, there is no disclosure or suggestion of a combination of metformin and glipizide.

There is no disclosure or suggestion in Patel et al. of a tablet which includes a combination of metformin and glipizide. In addition, there is no disclosure or suggestion in Patel et al. of a tablet which must be prepared in a manner to include 2 to 3% moisture to leave the metformin sufficiently compressible so that tablets may be formed while ensuring that the water content is not greater than

3% so that the glipizide (employed in combination with the metformin) will not hydrolyze and the water content is not less than 2% so that tablets can be made by compression and will not be subject to undesirable capping.

Furthermore, Patel et al. include their pharmaceutical active ingredient in the encapsulation coat while Appellants employ the metformin and glipizide in the tablet core.

For the above reasons, it is clear that Appellants' composition as claimed is patentable over Patel et al. taken alone.

U.S. Patent No. 6,303,146 to Bonhomme et al. relates to a solid oral dosage form containing a combination of metformin and glibenclamide, and not glipizide as is required in Appellants' formulation. Bonhomme et al. is primarily concerned with the preparation of a glibenclamide where the glibenclamide and metformin combination has a unique particle size distribution – at most 10% of the particles are less than 3 $\mu$ m and at most 10% of the particles are greater than 60 $\mu$ m. (Col. 2, lines 45 to 60). Appellants are not using glibenclamide and do not need a special particle size distribution for glipizide.

The Examiner refers to Col. 6, lines 37-49 of Bonhomme "to demonstrate routine knowledge in the art in determining 2-3% w/w moisture content prior to 'tableting'."

Bonhomme et al. teach that there was a loss of 2-3% w/w on drying. However, there is no disclosure or suggestion of a tablet containing metformin and glipizide containing 2-3% by weight moisture. There is nothing in Bonhomme et al. which would suggest to one skilled in the art to prepare a tablet containing a combination of metformin and glipizide. Appellants' do not need or use a special particle-sized glipizide. Accordingly, it is submitted that Appellants' invention as claimed is patentable over Bonhomme et al. taken alone.

It is also submitted that Appellants' invention as claimed is patentable over a combination of Chen et al. taken with Patel et al. and Bonhomme et al.

Chen et al. teaches a sustained release tablet which contains a combination of metformin and glipizide in a tablet core which is coated with a seal coating (optional) and a sustained release coating which is an enteric coating since it releases drug in the intestines (this cannot be present in Appellants' tablet). Appellants' composition includes the outer protective coating but does not include the Chen et al. sustained release coating (which is an enteric coating). Chen et al. disclose a loss on drying of less than 2%. Appellants' composition must include at least 2% moisture but no

more than 3% moisture. Chen et al. is totally devoid of Appellants' inventive concept as defined in Claim 1, that is a pharmaceutical composition which does not include an enteric or sustained release coating and which includes from 2 to 3% moisture which allows the metformin to be compressible to enable tablet formation without capping but which will not cause hydrolysis of the glipizide. The above differences are material and unobvious. Patel et al. adds nothing to Chen et al. which would make Appellants' composition obvious. Patel et al. does not disclose a pharmaceutical composition containing a combination of metformin and glipizide. Patel et al. does not address the moisture problem employing metformin and glipizide in a single formulation and how to solve it. Patel et al. disclose employing an encapsulation coat which will contain the active component whereas Appellants employ the metformin and glipizide in the tablet core composition. A combination of Chen et al. and Patel et al. would merely suggest to or motivate one skilled in the art to include a drug in the enteric coating of Chen et al. and do nothing about moisture content. Bonhomme et al. suggests 2-3% moisture in a composition containing metformin and specially sized particles of glibenclamide, not glipizide. At best the rejection of the claims is based on modifying the Chen et al. enteric coated sustained release tablet, using hindsight in view of Appellants' disclosure, so as to completely change its basic nature to omit the sustained release or enteric coating. The latter would, of course, be improper as lacking any foundation, in fact. There is nothing in either Chen et al., Patel et al. and/or Bonhomme et al. that would suggest that Chen et al. should be so modified. Thus, it is submitted that Appellants' invention as claimed is patentable over the combination of Chen et al. taken in view of Patel et al. and Bonhomme et al.

Absent the use of hindsight in view of Appellants' disclosure, there would be no reason for one skilled in the art reading the cited references to combine these references. The use of hindsight in view of Appellants' disclosure in combining references to reject Appellants' claims is clearly improper in view of In re Pye et al., 148 U.S.P.Q. 426 (CCPA 1966), ACS Hospital Systems, Inc. v. Montefiore Hospital, supra; and W.L. Gore & Assoc., Inc. v. Garlock, Inc., supra.

#### (7A) SUMMARY OF ARGUMENTS

Summing up, it is submitted that Appellants' invention as claimed is patentable over a combination of Chen et al., taken in view of Patel et al. and Bonhomme et al. Even if the techniques of the cited references were combined, the combination would not disclose or suggest to one skilled

in the art reading the cited references a tablet containing a combination of metformin and glipizide which contains 2-3% moisture and which is not a controlled release tablet. Accordingly, it is submitted that the cited combination of references are no more relevant than each taken alone and do not make Appellants' tablet as claimed obvious.

In applying the criteria for patentability as enunciated in Graham v. John Deere Co., supra, it is seen that:

- (1) the scope of the content of the prior art has been reviewed above.
- (2) the differences between the invention and the prior art have been set out, namely, that the prior art does not disclose or suggest a tablet containing metformin and glipizide which must contain 2 to 3% moisture to ensure tablet integrity and stability of glipizide.
- (3) the level of ordinary skill in the art is exceedingly high and involves scientists having Masters, Ph.D. and M.D. degrees.

It is submitted that there is no disclosure or suggestion in any of the cited references or combination thereof of the claimed composition. Absent the use of hindsight in view of Appellants' disclosure, there would be no reason for one skilled in the art reading the cited references to combine these references. The use of hindsight in view of Appellants' disclosure in combining references to reject Appellants' claims is clearly improper in view of In re Pye et al., 148 U.S.P.Q. 426 (CCPA 1966), ACS Hospital Systems, Inc. v. Montefiore Hospital, supra.; and W.L. Gore & Assoc., Inc. v. Garlock, Inc., supra.

#### (7B) CONCLUSION

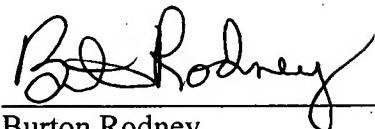
The Examiner has not established any factual basis sufficient to support the Examiner's conclusions and thus establish a prima facie case for obviousness of Appellants' invention as claimed. In re Piasecki, 745 F.2d 1468, 223 U.S.P.Q. 785 (Fed. Cir. 1984). In essence, the Examiner has merely alleged that the differences between Appellants' invention and the cited art are obvious, but has not set forth any basis in logic or scientific principle to support such contention as required under In re Soli, 317 F.2d 941, 127 U.S.P.Q. 797 (CCPA 1963). The very combination of references is improper as being based on hindsight in view of Appellants' disclosure.

In view of the fact that Appellants' invention as defined in Claims 1 and 11 to 16 of this application, is neither disclosed nor suggested in or made obvious by the cited prior art, it is

submitted that Appellants have shown that their invention as claimed is not anticipated by and is clearly patentable over the cited combination of references. Therefore, it is believed that the Examiner's final rejection of the claims on appeal should be reversed and that such claims should be allowed.

Appellants hereby waive an oral hearing.

Respectfully submitted,



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(8) CLAIMS APPENDIX  
(CLAIMS ON APPEAL)

Claim 1. A pharmaceutical composition comprising a single dosage formulation of metformin and glipizide said formulation containing from 2 to 3 % by weight moisture, said formulation being in the form of a tablet designed to control moisture so that the glipizide does not hydrolyze and said metformin is compressible, said tablet further including an outer protective coating or finishing layer surrounding said tablet, said composition being devoid of an enteric coating.

Claim 11. The pharmaceutical formulation as defined in Claim 1 which includes a dosage of metformin of from about 250 to about 2500 mg/day and a dosage of glipizide from about 1.25 to about 25 mg/day.

Claim 12. The pharmaceutical formulation as defined in Claim 1 wherein the metformin is employed in a weight ratio to the glipizide within the range from about 1000:1 to about 100:1.

Claim 13. The pharmaceutical formulation as defined in Claim 1 wherein the dosage of metformin is 250 mg and the dosage of glipizide is 1.25 mg.

Claim 14. The pharmaceutical formulation as defined in Claim 1 wherein the dosage of metformin is 250 mg and the dosage of glipizide is 2.50 mg.

Claim 15. The pharmaceutical formulation as defined in Claim 1 wherein the dosage of metformin is 500 mg and the dosage of glipizide is 2.50 mg.

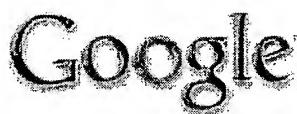
Claim 16. The pharmaceutical formulation as defined in Claim 1 wherein the dosage of metformin is 500 mg and the dosage of glipizide is 5.00 mg.

**(9) EVIDENCE APPENDIX**

None.

**(10) RELATED PROCEEDINGS APPENDIX**

None.

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enteric coating. A protective coating that allows a pill to pass intact through the stomach and into the small intestine, where the coating dissolves and ...

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**pH-sensitive, enteric coated tablet**

Since capsules can not be enteric coated, any enzyme formula in a capsule ... Also beware of the term " enteric coated ". An enteric coating is a coating ...

[www.bluegrass.net/~jclark/ph\\_sensitive.htm](http://www.bluegrass.net/~jclark/ph_sensitive.htm) - 8k -

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**Enteric coating - Wikipedia, the free encyclopedia**

An enteric coating is a barrier applied to oral medication that controls the ... Enteric coating can also be used to prevent the acidic environment of the ...

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the effects of aspirin, buffered aspirin, and enteric-coated. aspirin on gastric and duodenal ... findings after treatment with enteric-coated and plain ...

[www.ualberta.ca/~csps/JPPS2\(1\)/N.Davies/NSAID-Davies.pdf](http://www.ualberta.ca/~csps/JPPS2(1)/N.Davies/NSAID-Davies.pdf) -

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Nutrateric™ is an aqueous enteric coating system designed specifically to meet the regulatory requirements for dietary supplement products marketed in the ...

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[www.idealcures.co.in/entericcoating.htm - 30k -](http://www.idealcures.co.in/entericcoating.htm - 30k -) Cached - Similar pages

### **Look What I Found In My Brain!: enteric coating**

An **enteric coating** is a **coating** put on a pill or capsule so that it doesn't dissolve until it reaches the small intestine. While the **coating** may make a pill ...  
[www.sff.net/people/lucy-snyder/ brain/2005/07/enteric-coating.html - 30k -](http://www.sff.net/people/lucy-snyder/ brain/2005/07/enteric-coating.html - 30k -) Cached - Similar pages

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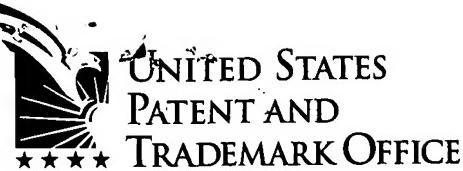
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